Complete Summary

GUIDELINE TITLE

Depression.

BIBLIOGRAPHIC SOURCE(S)

University of Michigan Health System. Depression. Ann Arbor (MI): University of Michigan Health System; 2004 May. 21 p. [3 references]

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: University of Michigan Health System. UMHS clinical care guideline: depression. Ann Arbor (MI): University of Michigan Health System; 1998. 14 p.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Depression including:

- Major depressive disorder
- Minor depression
- Dysthymia
- Seasonal affective disorder
- Mood disorders associated with a general medical condition

GUIDELINE CATEGORY

Diagnosis
Management
Screening
Treatment

CLINICAL SPECIALTY

Family Practice
Internal Medicine
Obstetrics and Gynecology
Psychiatry
Psychology

INTENDED USERS

Physicians
Psychologists/Non-physician Behavioral Health Clinicians
Social Workers

GUIDELINE OBJECTIVE(S)

- To improve the early recognition and treatment of depression in the primary care setting
- To familiarize clinicians with appropriate treatment options, drug side effects, and interactions
- To improve patient's understanding of depression as a treatable illness
- To identify when referral is indicated

TARGET POPULATION

Adults with depressive disorders

INTERVENTIONS AND PRACTICES CONSIDERED

Screening and Diagnosis

1. Patient Health Questionnaire (PHQ-9)
2. History
3. Evaluation
4. Physical examination
5. Laboratory testing

Treatment

1. Supportive care:
    - Patient Education
    - Exercise
2. Pharmacotherapy:
    - Selective Serotonin Reuptake Inhibitors (SSRIs)
        - citalopram (Celexa)
        - escitalopram (Lexapro)

        - fluoxetine (Prozac, Sarafem, Prozac Weekly)
        - paroxetine (Paxil, Paxil CR)
        - sertraline (Zoloft)
    - Serotonin-2 Antagonist/Reuptake Inhibitor
        - nefazodone (Serzone)
    - Serotonin/Norepinephrine Reuptake Inhibitor (SNRIs)
        - venlafaxine (Effexor XR)
        - duloxetine (Cymbalta)
    - Serotonin & alpha-2 Receptor Blocker
        - mirtazapine (Remeron)
    - Norepinephrine/Dopamine Reuptake Inhibitor
        - bupropion (Wellbutrin SR, Wellbutrin XL, Wellbutrin IR)
3. Psychotherapy:
    - Any psychotherapy
    - Interpersonal psychotherapy (IPT)
    - Cognitive behavioral psychotherapy (CBT)
    - Marital therapy
4. Treatments for severe or refractory depression:
    - Electroconvulsive therapy, monoamine oxidase inhibitors (MAOIs), lithium, thyroid hormone supplementation, valproic acid, antidepressant augmentation, stimulant medication, referral
5. Controversial Areas (No specific recommendations made)
    - St. John's Wort (hypericum perforatum)
    - Withdrawal syndrome

MAJOR OUTCOMES CONSIDERED

- Mortality rates by suicide
- Depressive symptoms
- Time to respond to pharmacotherapy
- Frequency and severity of relapses
- Outpatient visits and inpatient hospitalization
- Mortality from myocardial infarction
- Direct and indirect costs (including direct patient care, time lost from work, and potential income loss due to suicide) associated with major depressive disorder

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

The literature search for this update began with results of the literature search performed in 1997 to develop the initial guideline. The literature search conducted in 2002 for this project was conducted prospectively on Medline using the major keywords of depression, depressive disorders; consensus development conferences, practice guidelines, guidelines, outcomes and process assessment (health care); clinical trials, controlled clinical trials, multicenter studies,

randomized controlled trials, cohort studies; adults; English language; and published between 1/1/97 and 9/30/02.

Terms used for specific topic searches within the major key words included: epidemiology; national cost of treatment (economics); screening (for depression, bipolar disorder; alcohol abuse); diagnosis; suicide risk assessment; patient education; exercise; serotonin selective reuptake inhibition (citalopram, escitalopram, fluoxetine, paroxetine, sertraline), serotonin/norepinephrine reuptake inhibition (duloxetine, mirtazapine, tricyclic antidepressants, venlafaxine), norepinephrine/dopamine reuptake inhibition (bupropion), serotonin-2 antagonist/reuptake inhibition (nefazodone, trazodone), St. John´s Wort (Hypericum Perforatum), maintenance on pharmacotherapy, continuation duration, withdrawal syndrome (paroxetine/Paxil), medication adherence, managing sexual side effects of pharmacologic agents, pregnancy and pharmacologic agents, breast feeding and pharmacologic agents, pharmacotherapy not included above; interpersonal psychotherapy, cognitive behavioral therapy, short-term or focal psychodynamic psychotherapy, marital therapy, psychotherapy, not included above; other treatment not included above; ongoing clinical assessment; medical comorbidity, alcohol abuse, panic (including generalized anxiety disorder or phobia), obsessive compulsive disorder, eating disorders and anorexia nervosa, partner violence, sexual assault, pregnancy (not included above), postpartum (not included above); and depression not included above.

The search was conducted in components each keyed to a specific causal link in a formal problem structure (available upon request). The search was supplemented with very recent clinical trials known to expert members of the panel. Negative trials were specifically sought. The search was a single cycle.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Levels of evidence for the most significant recommendations:

A. Randomized controlled trials
B. Controlled trials, no randomization
C. Observational trials
D. Opinion of expert panel

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Consideration of benefits, harms, costs, and patient preferences.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

Pharmaceutical cost data were reviewed (see Table 5 in the original guideline document).

METHOD OF GUIDELINE VALIDATION

Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

University of Michigan Health System (UMHS) guidelines are reviewed by leadership in departments to which the content is most relevant. This guideline concerning depression was reviewed by members of the following departments: Family Medicine; General Medicine; Obstetrics and Gynecology; and Psychiatry.

Guidelines are approved by the Primary Care Executive Committee (PCEC) and the Executive Committee of Clinical Affairs (ECCA).

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Note from the National Guideline Clearinghouse (NGC): The following key points summarize the content of the guideline. Refer to the original guideline document for additional information. The levels of evidence [A-D] are defined at the end of the "Major Recommendations" field.

Diagnosis

Depressed patients frequently present with somatic complaints to their primary care doctor rather than complaining of depressed mood [C].

Treatment

Mild depression can be effectively treated with either medication or psychotherapy. Moderate to severe depression may require an approach combining medication and psychotherapy [A].

- Drug treatment. Fifty to sixty-five percent (50–65%) of patients respond to the first antidepressant [A]. No particular antidepressant agent is superior to another in efficacy or time to response. Choice can be guided by matching patients' symptoms to side effect profile, presence of medical and psychiatric comorbidity, and prior response [A]. Relative costs can also be considered (e.g., generics). University of Michigan Health System (UMHS) preferred agents are Fluoxetine (generic) and citalopram (Celexa®). Patients treated with antidepressants should be closely observed for possible worsening of depression or suicidality, especially at the beginning of therapy or when the dose increases or decreases [C].
- Frequent initial visits. Patients require frequent visits early in treatment to assess response to intervention, suicidal ideation, side effects, and psychosocial support systems [D].
- Continuation therapy. Continuation therapy (9–12 months after acute symptoms resolve) decreases the incidence of relapse of major depression [A]. Long term maintenance or life-time drug therapy should be considered for selected patients based on their history of relapse and other clinical features [B].
- Education/support. Patient education and support are essential. Social stigma and patient resistance to the diagnosis of depression continue to be a problem [D].

Definitions:

Levels of Evidence

A. Randomized controlled trials
B. Controlled trials, no randomization
C. Observational trials
D. Opinion of expert panel

CLINICAL ALGORITHM(S)

An algorithm is provided in the original guideline document for an overview of treatment for depression.

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for each recommendation (see "Major Recommendations").

Conclusions were based on prospective randomized clinical trials (RCTs) if available, to the exclusion of other data; if RCTs were not available, observational

studies were admitted to consideration. If no such data were available for a given link in the problem formulation, expert opinion was used to estimate effect size.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

- Timely recognition and accurate diagnosis of depression
- Appropriate treatment of depression, with accompanying improvement in patient mood and functioning
- Appropriate continuation and maintenance therapy to decrease the incidence of relapse of major depression
- Cost-effective prescription of antidepressant medications

Subgroups Most Likely to Benefit

Patient profiles most likely to benefit from selected antidepressants:

- Citalopram: elderly patient, patient with an agitated depression, or patient with gastrointestinal (GI) distress/sensitivity
- Escitalopram: elderly patient, patient with an agitated depression, or patient with GI distress/sensitivity
- Fluoxetine: noncompliant or "forgetful" patient; excessive fatigue
- Paroxetine: less likely to produce initial anxiety and/or insomnia; controlled release version is less likely to produce initial nausea
- Sertraline: the medical surgical patient on one or more medical drugs; initial activation and increased alertness desired
- Nefazodone: the depressed over-anxious patient with marked difficulty sleeping
- Venlafaxine: patients with menopausal symptoms or failing a selective serotonin reuptake inhibitor (SSRI) trial; at higher doses patients with chronic pain
- Duloxetine: patient with depression and chronic pain; patient failing an SSRI trial
- Mirtazapine: the medically ill patient with weight loss, insomnia, and nausea
- Bupropion: the now depressed, actually or potentially bipolar patient; the apathetic, low energy patient; patients motivated to stop smoking, patients with attention deficit hyperactivity disorder (ADHD)

POTENTIAL HARMS

Side effects associated with pharmacotherapy: insomnia, akathisia (a syndrome characterized by muscle restlessness), weight gain and sexual dysfunction.

- Citalopram: may be initially sedating or initially increase alertness; mild initial sedation is dose-dependent; sexual dysfunction common
- Escitalopram: sexual dysfunction common
- Fluoxetine: tends to produce more initial nervousness and arousal than other selective serotonin reuptake inhibitors (SSRIs); sexual dysfunction common

- Paroxetine: tends to cause fewer arousal and insomnia effects common with SSRIs; possesses some anticholinergic effects; sexual dysfunction common
- Sertraline: tends to increase alertness; sexual dysfunction common
- Nefazodone: BLACK BOX WARNING: Liver damage and/or liver failure in 1/250,000 patients; fatigue and dizziness; sexual dysfunction unlikely.
- Venlafaxine: common side effects to all SSRIs with more nausea; sustained hypertension risk; blood pressure increases are dose-dependent; constipation; sexual dysfunction less common.
- Duloxetine: similar to SSRIs, but more exaggerated; mild blood pressure elevations; nausea, dry mouth, somnolence, and constipation; sexual dysfunction less common.
- Mirtazapine: produces sleep; lower doses produce more sleep than do higher doses; weight gain; sexual dysfunction unlikely.
- Bupropion: most activating antidepressant available; sexual dysfunction rare.

Subgroups Most Likely to be Harmed:

Patient profiles least likely to benefit from selected antidepressants:

- Citalopram: elderly patient with excessive sleep and apathy
- Escitalopram: elderly patient with excessive sleep and apathy
- Fluoxetine: patient on several medications and/or frequent medication changes anticipated
- Paroxetine: patients who may require high doses or elderly are more prone to anticholinergic effects (e.g., delirium)
- Sertraline: patients sensitive to any of the typical SSRI side-effects (e.g., increased arousal)
- Nefazodone: patients who sleep excessively with life-long underachievement and excessive contentment
- Venlafaxine: patients with unstable blood pressure and perhaps, those with gastrointestinal (GI) sensitivity
- Duloxetine: patient with significant anorexia, constipation, or other GI symptoms
- Mirtazapine: the obese patient with fatigue and hypersomnia; patients with neutropenia
- Bupropion: patients who are agitated, very anxious, and/or panicky; patients at risk for seizures and/or with history of head trauma, substance abuse, eating disorder, or electrolyte disturbance

CONTRAINDICATIONS

CONTRAINDICATIONS

- Do not combine any of the listed antidepressants with monoamine oxidase inhibitors (MAOIs).
- Rare case reports suggest the potential for a patient taking serotonergic antidepressants to develop a serotonin syndrome (altered mental status, agitation, myoclonus, hyperreflexia) with the concomitant use of buspirone, dextromethorphan, tramadol, St. John's Wort, and the triptan class of drugs (used for migraine headache). However, the clinical significance of this risk is unclear and probably extremely low.

- DO NOT USE bupropion (Wellbutrin) if history of seizure, head trauma, substance abuse, bulimia, anorexia or electrolyte disturbance.
- Selected Important Drug/Drug Interactions:
    - Citalopram: minimal inhibitor of CYP 2D6 isoenzymes; good choice for medical /surgical patients without renal impairment
    - Escitalopram: comparable to citalopram
    - Fluoxetine: potent inhibitor of CYP 2D6 isoenzymes; increases risk of phenytoin (Dilantin) toxicity.
    - Paroxetine: potent inhibitor of CYP 2D6 isoenzymes
    - Sertraline: weak inhibitor of CYP 2D6 isoenzymes; Good choice for medical/surgical patients; contraindicated with pimozide (Orap)
    - Nefazodone: moderate inhibitor of CYP3A3/4 and p-glycoprotein; causes 15% reduction in oral clearance of digoxin; contraindicated with cyclosporine, simvastatin (Zocor) and many other statins, pimozide (Orap), and sildenafil (Viagra)
    - Venlafaxine: usually clinically insignificant due to low protein binding and weak inhibition of P450 enzymes
    - Duloxetine: insufficient information
    - Mirtazapine: usually clinically insignificant due to extensive metabolism via CYP1A2, 2D6, 3A4; does not appear to interfere with the metabolism of other drugs
    - Bupropion: metabolized primarily by CYP2B6; drugs inhibiting CYP2B6 are not currently identified; recent report finds that bupropion may cause clinically significant inhibition of CYP2D6.
- Marital therapy should only be considered if violence is screened for and absent in the relationship.

QUALIFYING STATEMENTS

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These guidelines should not be construed as including all proper methods of care or excluding other acceptable methods of care reasonably directed to obtaining the same results. The ultimate judgment regarding any specific clinical procedure or treatment must be made by the physician in light of the circumstances presented by the patient.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

IMPLEMENTATION TOOLS

Clinical Algorithm
Patient Resources

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Getting Better
Living with Illness

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

University of Michigan Health System. Depression. Ann Arbor (MI): University of Michigan Health System; 2004 May. 21 p. [3 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

1998 Jun (revised 2004 May)

GUIDELINE DEVELOPER(S)

University of Michigan Health System - Academic Institution

SOURCE(S) OF FUNDING

Internal funding for UMHS guidelines is provided by the Office of Clinical Affairs. No external funds are used.

GUIDELINE COMMITTEE

Depression Guideline Team

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

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Guidelines Oversight Team: Connie Standiford, MD; Lee Green, MD, MPH; R. Van Harrison, PhD

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

The University of Michigan Health System endorses the Guidelines of the Association of American Medical Colleges and the Standards of the Accreditation Council for Continuing Medical Education that the individuals who present educational activities disclose significant relationships with commercial companies whose products or services are discussed. Disclosure of a relationship is not intended to suggest bias in the information presented, but is made to provide readers with information that might be of potential importance to their evaluation of the information.

Team Member/Relationship/Company

Thomas Schwenk, MD (None)
Linda Terrell, MD (None)
Van Harrison, PhD (None)
Elizabeth Shadigian, MD (None)
Marcia Valenstein, MD (Research Grant: Pfizer)

GUIDELINE STATUS

This is the current release of the guideline.

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GUIDELINE AVAILABILITY

Electronic copies: Available for download in Portable Document Format (PDF) from the University of Michigan Health System Web site.

AVAILABILITY OF COMPANION DOCUMENTS

None available

PATIENT RESOURCES

The following is available:

- Depression: symptoms and treatment patient education handout. University of Michigan Health System; 2003 Dec. Various p.

Electronic copies: Available from the University of Michigan Health System Web site.

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By

providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC STATUS

This summary was completed by ECRI on May 20, 1999. The information was verified by the guideline developer on June 17, 1999. This NGC summary was updated by ECRI on October 12, 2004. The updated information was verified by the guideline developer on October 22, 2004.

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